

REMARKS

Claims 1-22 are pending. Claims 5 and 10-20 stand withdrawn from consideration as a non-elected invention under a restriction requirement. By the present amendment, claims 1, 3, 4, 9 and 21 are amended and claim 22 is canceled.

Election/Restriction

The Office Action asserts that claims 5 and 10-20 are withdrawn due to there being no allowable generic or linking claim. The applicant respectfully submits that the claims, as currently amended, recite a CXCR4 antagonist including SDF-1[P2G] (SEQ ID NO: 1) or a fragment or analog thereof, or including 3-hydroxy-2-napthoic acid and are allowable and generic to the claimed species. Accordingly, the applicant respectfully requests rejoinder of the withdrawn claims.

Priority

As requested, enclosed is a certified copy of Canadian Application No. 2,305,787. Also enclosed is a newly executed Declaration, signed by inventors Merzouk and Salari, and unambiguously stating the foreign priority claim. Declarations signed by the remaining inventors will be forwarded as soon as they are available.

With respect to claim 22, the applicant respectfully submits that the prior applications provide sufficient support to comply with the requirements of 35 U.S.C. § 112, first paragraph, and therefore the claim is entitled to the priority dates of the parent provisional and earlier Canadian applications. However, as discussed below, claim 22 has been canceled to expedite prosecution and therefore this objection is not addressed further herein.

Objection

Claim 9 is objected to as being directed in part to non-elected subject matter. In response, claim 9 has been amended to delete the non-elected subject matter. The applicant reserves the right to reintroduce the deleted subject matter upon notification of an allowable or generic linking claim.

Rejections Under 35 U.S.C. § 112

The specification is objected to and the claims rejected under 35 U.S.C. § 112, first paragraph, on the basis, according to the applicant's understanding, that the specification does not provide an adequate written description of the invention. More specifically, the Office Action asserts that the applicant does not describe CXCR4 antagonists other than peptides including the first 9 amino acids of SDF-1 and having a glycine substituted for proline at position 2 of the native peptide or the small molecule set forth on page 29 of the specification.

Claims 1, 3, and 21, the independent claims, have been amended to recite a CXCR4 antagonist including a SDF-1 molecule having a mutation changing P to G at position 2(SDF-1[P2G]; SEQ ID NO: 1) or a fragment or analog thereof, or including 3-hydroxy-2-napthoic acid. Support for this amendment may be found, for example, at pages 15 to 26 and throughout the specification. The Office Action, citing MPEP 2163(ii), states that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics. In the present case, the specification exhaustively describes and reduces to practice a large number of species representing the claimed genus of SDF-1 molecules having a glycine substituted for proline at position 2, and fragments and analogs thereof (see, for example, the specification at pages 15- to 26). In addition, the specification discloses relevant identifying characteristics of molecules corresponding to the claimed genus, such as, the ability to bind CXCR4 and exhibit CXCR4 antagonist activity (see, for example, pages 49 to 52).

In response to the assertion that the specification “does not teach the relevant identifying characteristics of a peptide antagonist of CXCR4 which does not at least comprise the first 9 amino acids of SDF-1” (Office Action, page 5), the applicant respectfully submits that the specification describes a variety of fragments and analogs of SDF-1[P2G], including molecules having fewer than (or other than) the first 9 amino acids of SDF-1. For example, the specification describes sequences including the first 8 amino acids of SDF-1[P2G] (see, for example, page 17); sequences having specified substitutions at positions 5, 6, 7, or 8 of SDF-1[P2G] (see, for example, pages 16 to 18); and sequences including specified SDF-1 motifs (see, for example, page 21).

Furthermore, the applicant respectfully submits that the specification does more than simply describe “a variety of methods by which CXCR4 antagonists might be identified,” as is asserted by the Office Action. As discussed herein, the specification describes in great detail the sequence and structure of a large number of SDF-1[P2G] analogs and fragments and thus fully complies with the written description requirement. Accordingly, the applicant respectfully submits that claims reciting CXCR4 antagonists including a SDF-1 molecule having a mutation changing P to G at position 2(SDF-1[P2G]; SEQ ID NO: 1) or a fragment or analog thereof satisfy the written description requirement.

The claims also stand rejected under 35 U.S.C. § 112, first paragraph, on the basis, according to the applicant's understanding, that the specification is not enabling. More specifically, the Office Action contends that demonstration of a method of promoting the rate of BFU-E or CFU-GM multiplication does not enable a method of promoting proliferation of all hematopoietic cells. The Office Action cites Hodohara et al. (Blood 95: 769-775, 2000; hereafter “Hodohara”), asserting that Hodohara discloses that SDF-1 stimulates growth of bone marrow progenitor cells and thus teaches away from the instant invention, and concluding that the state of the art at the time of filing of the instant invention would prevent a skilled person from knowing how to obtain a proliferative response from all hematopoietic cells using the methods of the instant invention. The Office Action further asserts that the guidance in the specification is inadequate, alleging that the specification, at Figure 2, teaches that CXCR4 antagonists had no effect on the cycling status of long-term culture initiating cells and thus teaches that the methods of the instant invention do not work for all hematopoietic cells. Thus, the Office Action concludes that given the large genus of hematopoietic cells and the limited number of working examples, undue experimentation would be required to practice the claimed invention.

This rejection is respectfully traversed. The present invention provides, in part, methods of promoting the rate of hematopoietic cell multiplication or increasing the circulation of hematopoietic cells by administering a CXCR4 antagonist including a SDF-1 molecule having a mutation changing P to G at position 2 (SDF-1[P2G]; SEQ ID NO: 1) or a fragment or analog thereof or including 3-hydroxy-2-napthoic acid, as currently claimed. In support of the claims, the specification describes such CXCR4 antagonists in detail (for example, at pages 15 to 26 and page 29) and teaches promoting the rate of hematopoietic cell multiplication and increasing the circulation of hematopoietic cells by exemplary CXCR4 antagonists using different hematopoietic cells (see, for example, pages 49 to 52). These results demonstrate that a wide variety of the claimed CXCR4 antagonists are capable of being used in more than one hematopoietic cell type according to the methods of the invention.

In contrast, Hodohara discloses that “SDF-1, acts together with TPO [thrombopoietin] to stimulate megakaryocyte colony growth from bone marrow progenitor cells” (page 773, emphasis added), while “SDF-1 alone did not support the growth of megakaryocyte colonies from marrow cells” (page 770). Hodohara simply documents the results of experiments conducted using a combination of native SDF-1 and TPO and merely notes a lack of response in the experiments where SDF-1 alone was used. Hodohara’s teachings therefore cannot be considered an indicator of the state of the art, or be used to draw conclusions regarding the efficacy or enablement of the instant invention, because Hodohara does not teach or disclose the effects of a CXCR4 antagonist, as presently claimed, on the multiplication or circulation of hematopoietic cells.

Turning to the assertion that Figure 2 of the specification teaches that CXCR4 antagonists had no effect on the cycling status of long-term culture initiating cells, the applicant respectfully submits that Figure 2 is merely an embodiment of an alternative aspect of the invention, representing as it does a single experiment conducted under a single set of conditions. Therefore, Figure 2 does not provide a basis for either an assertion that the methods of the invention will not work in connection with long-term culture initiating cells in particular, or hematopoietic cells, other than BFU-E or CFU-GM cells, in general. Thus, the applicant respectfully submits that claims reciting hematopoietic cells are fully enabled according to the methods of the invention.

Claim 4, which is directed to a method of promoting the rate of hematopoietic cell multiplication by introducing a heterologous gene into the hematopoietic cells for gene therapy, stands rejected under 35 U.S.C. § 112, first paragraph, on the basis, according to the applicant's understanding, that the specification is not enabling. More specifically, the Office Action asserts that the specification does not set forth any specific conditions to be treated according to the claimed method, thus encompassing a general method of treating any condition by gene therapy, and cites references teaching that multiple problems remain to be solved in gene therapy techniques.

This rejection is respectfully traversed. Claim 4 is a dependent claim and therefore by definition incorporates all the limitations of claim 1. Claim 1 recites a method of promoting the rate of hematopoietic cell multiplication. Thus, claim 4 is necessarily directed to a gene therapy method by which hematopoietic cell multiplication may be promoted and is therefore directed to a condition that would benefit from hematopoietic cell multiplication. The specification at, for example, page 46, lists examples of such conditions as being "blood transfusion or engraftment, host conditioning or applications relevant to chemotherapy, radiation therapy or myeloablative therapy." Thus, the specification makes clear the types of conditions intended to be treated according to the claimed method. For further clarification, claim 4 has been amended to recite that the claimed heterologous gene encodes a SDF-1[P2G] (SEQ ID NO: 1) molecule or a fragment or analog thereof, and that the gene therapy is for promoting the rate of hematopoietic cell multiplication. Support for this amendment may be found, for example, at page 46 of the specification.

With respect to the assertion that undue experimentation is required to practice gene therapy according to the methods of the invention, the Office Action relies on a number of references to assert that the field of gene therapy is unpredictable and that gene therapy had not been successfully practiced at the time of the invention, stating that "even in an area of gene therapy considered promising, significant obstacles to successful gene therapy remained well after the effective filing date of the instant application" (Office Action, page 14). The applicant respectfully submits that such a statement is tantamount to stating that any claim pertaining to gene therapy is automatically in a suspect field and that, absent proof of completely reliable cures in human patients, there can be no patents in the field of gene therapy. In so doing, the Office Action applies a standard of perfection that is not found in the statute or the case law.

The standard for enablement is that the specification be enabling to a person “skilled in the art to which it pertains or with which it is most nearly connected.” (MPEP 2164.05(b)). The level of skill, in the art of gene therapy, is generally high and even if the applicant were to agree with the Office Action that some experimentation may be required to practice the invention as claimed, the applicant submits that any such experimentation is not undue or unreasonable, which is the applicable standard (M.P.E.P § 2164.01). Even complex experimentation, involving an extended period of time and expense, is not necessarily undue if the experimentation is routine and the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed (M.P.E.P §§ 2164.01, 2164.06). In the present case, the novelty of the present invention lies, in part, in the use of the claimed CXCR4 antagonists to promote the rate of hematopoietic cell multiplication. Use of the claimed CXCR4 antagonists in gene therapy methods is an alternative embodiment of the invention which is discussed in detail in the specification at, for example, pages 44 to 47. Thus, the specification provides sufficient guidance to enable a skilled person to practice the methods of the invention in gene therapy techniques, and this guidance is not negated by assertions that gene therapy is an emerging technology.

Claims 21 and 22 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis, according to the applicant's understanding, that they are indefinite. More specifically, the Office Action asserts that the claims do not set forth a terminal process step that clearly relates back to the preamble. In addition, the Office Action asserts that, with respect to claim 22, the specification does not provide a basis for therapeutic efficacy in the treatment of autoimmune disease based on hematopoietic cell multiplication.

Claim 21 has been amended to recite a terminal process step. Support for this amendment may be found in the specification at, for example, page 47, lines 7 to 27. Claim 22 has been canceled and therefore this rejection is moot.

Applicant submits that all rejections under 35 U.S.C. § 112 have been addressed and respectfully requests that the Examiner not renew claim rejections under 35 U.S.C. § 112.

Rejection Under 35 U.S.C. 103

Claim 22 stands rejected under 35 U.S.C. §103(a) for obviousness over art cited in the Office Action. While applicant respectfully submits that the cited art does not render claim 22 obvious, claim 22 has been canceled to expedite prosecution of the currently pending claims and therefore this rejection is moot. Applicant reserves the right to pursue the subject matter of claim 22 in a future related application.

CONCLUSION

In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,

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